



PATENT APPLICATION
Serial No. 08/519,293
Attorney Docket No. 1217-951551

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

Group Art Unit 1651 :
In re Application of :
Hitoshi NAGAOKA : **INHIBITOR OF HEPATITIS B**
Serial No. 08/519,293 : **AND HIV ACTIVITY**
Filed August 25, 1995 :
Examiner - I. Marx :
Pittsburgh, Pennsylvania
February 27, 2003

DECLARATION

Commissioner of Patents
Washington, D.C. 20231

I, Hideo Sawadaishi, declare as follows:

1. I am a citizen of Japan, and reside at 1-20-2-103, Todaijima, Urayasu-shi, Chiba-ken, Japan. I graduated from prefectural Shimizu School, Department of Industrial Chemistry in March 1975. From April 1975 through 1991, I was an employee of Noda Shokkin Kogyo K.K. where I engaged in various research and development projects concerning Lentinus edodes mycelium. Since 1991, I have been engaged in research and development projects concerning Lentinus edodes mycelium.

2. I have read and am thoroughly familiar with the contents of the above-identified patent application as well as of the prior art references cited in the application. I have read and I understand new claim 20.

3. In order to support further the unexpected results obtained from the Lentinus edodes mycelium extract of the present invention, my colleagues Kijuroh Nomura and Hitoshi Nagaoka conducted a scientific investigation in order to determine the effectiveness of the extract in treating patients with hepatitis B virus. I followed the scientific investigation closely at the time it was completed and have personal knowledge that the attached twenty pages are a true and correct summary of tests conducted and results achieved. The contents and significance of the attachment is summarized briefly below.

Method

Fifty-eight patients having acute or chronic hepatitis B were given 2 g daily of an Lentinus edodes mycelium extract powder, prepared according to claim 20, in the form of a drink. In particular, the extract was prepared by inoculating *Lentinus edodes* fungus in a solid culture medium comprising 90 parts by weight of bagasse and 10 parts by weight of rice bran to yield proliferated mycelium; disentangling the solid culture medium containing the proliferated mycelium so that the amount of the bagasse of 12-in mesh is not more than 30% by weight and adding thereto 1 to 10 kg of water and 0.5 to 5 g of at least one enzyme selected from the group consisting of cellulase, protease and glucosidase based on 1 kg of the disentangled solid culture medium, while keeping the solid culture medium at 30 to 50 ° C, to give a bagasse-containing mixture; grinding and milling the bagasse-containing mixture so that the amount of the bagasse of 12-in mesh is not less than 70% by weight; heating the ground and milled bagasse-containing mixture to a temperature of 75 to 95° C to inactivate the enzyme; filtering the resultant mixture through a filter cloth of 50 to 120-in mesh to thereby obtain a pharmaceutical

Lentinus edodes mycelium extract; and administering at least one effective dose of said extract to an animal or human afflicted with a viral disease. The patients' response to treatment were evaluated by measuring serum levels of GOT and GPT enzymes as well as serum levels of hepatitis B "e" (Hbe) antigens and antibodies (a known marker for hepatitis B virus infection).

Results

There was a highly significant response to Lentinus edodes mycelium extract treatment. Seventy-two percent of the patients seroconverted from Hbe antigen positivity to Hbe negativity, and responded with a 50% or more reduction in their GOT and GPT serum liver enzymes. Of the 72% of the patients that responded favorably to treatment, 15.5% of the patients had GOT and GPT values of 40 units or less, and the remaining 56.9% had GOT and GPT values of 100 or less. These patients also reported an improvement in their subjective symptoms. None of the patients in the study reported having any adverse side effects from the treatment or any worsening of symptoms.

Conclusion

A highly significant percentage of patients infected with hepatitis B, after daily treatment with the Lentinus edodes mycelium extract of the present invention, showed a remarkable improvement in their serum liver enzymes, which was accompanied by Hbe seroconversion from positive to negative, a subjective improvement in symptomatology, and a complete lack of adverse side effects. I also know from my expertise in the area of hepatitis B that hepatitis B patients, left untreated, do not undergo Hbe seroconversion to a highly significant percentage. I therefore conclude that the results of this patient study emphasize that claim 20 (i.e., the above-described method of making an extract and

administering an effective amount to a patient in need of treatment for a viral disease) recites a way of treating viral diseases which accomplishes new and unexpectedly efficacious results, as compared to conventional treatment or no treatment.

4. I declare further that all statements made herein of my own knowledge are true and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and any patent issuing thereon.

Hideo Sawadaishi
Hideo Sawadaishi

Date February 28, 2003